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=> dup rem l1
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L2 18 DUP REM L1 (12 DUPLICATES REMOVED)

=> dis ibib abs l2 1-18

L2 ANSWER 1 OF 18 EMBASE COPYRIGHT (c) 2008 Elsevier B.V. All rights
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ACCESSION NUMBER: 2008500137 EMBASE
TITLE: New Insights into the Mechanisms of Macroautophagy in
Mammalian Cells.
AUTHOR: Eskelinen, Eeva-Liisa (correspondence)
CORPORATE SOURCE: Division of Biochemistry, Department of Biological and
Environmental Sciences, University of Helsinki, Helsinki,
Finland.
SOURCE: International Review of Cell and Molecular Biology, (2008)
Vol. 266, pp. 207-247.
Editor: Jeon, Kwang
Refs: 197
ISSN: 1937-6448 ISBN: 9780123743725
PUBLISHER: Elsevier Inc., 360 Park Avenue South, New York, NY 10010,
United States.
PUBLISHER IDENT.: S 1937-6448(07)66005-5
COUNTRY: United States
DOCUMENT TYPE: Book; Series; (Book Series); General Review; (Review)
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
029 Clinical and Experimental Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 25 Nov 2008
Last Updated on STN: 25 Nov 2008

AB Macroautophagy is a self-digesting pathway responsible for the removal of
long-lived proteins and organelles by the lysosomal compartment. Parts of
the cytoplasm are first segregated in double-membrane-bound
autophagosomes, which then undergo a multistep maturation process
including fusion with endosomes and lysosomes. The segregated cytoplasm
is then degraded by the lysosomal hydrolases. The discovery of ATG genes
has greatly enhanced our understanding of the mechanisms of this pathway.
Two novel ubiquitin-like protein conjugation systems were shown to
function during autophagosome formation. Autophagy has been shown to play
a role in a wide variety of physiological processes including energy
metabolism, organelle turnover, growth regulation, and aging. Impaired

autophagy can lead to diseases such as cardiomyopathy and cancer. This review summarizes current knowledge about the formation and maturation of autophagosomes, the role of macroautophagy in various physiological and pathological conditions, and the signaling pathways that regulate this process in mammalian cells. .COPYRGT. 2008 Elsevier Inc. All rights reserved.

L2 ANSWER 2 OF 18 MEDLINE on STN
ACCESSION NUMBER: 2008611886 MEDLINE
DOCUMENT NUMBER: PubMed ID: 18690010
TITLE: A life-span extending form of autophagy employs the vacuole-vacuole fusion machinery.
AUTHOR: Tang Fusheng; Watkins Joseph W; Bermudez Maria; Gray Russell; Gaban Adam; Portie Ken; Grace Stephen; Kleve Maurice; Craciun Gheorghe
CORPORATE SOURCE: Department of Biology, University of Arkansas, Little Rock, Arkansas 72204-1099, USA.. fxtang@ualr.edu
SOURCE: Autophagy, (2008 Oct 1) Vol. 4, No. 7, pp. 874-86.
Electronic Publication: 2008-10-08.
Journal code: 101265188. E-ISSN: 1554-8635.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200811
ENTRY DATE: Entered STN: 20 Sep 2008
Last Updated on STN: 18 Nov 2008
Entered Medline: 17 Nov 2008

AB While autophagy is believed to be beneficial for life-span extension, it is controversial which forms or aspects of autophagy are responsible for this effect. We addressed this topic by analyzing the life span of yeast autophagy mutants under caloric restriction, a longevity manipulation. Surprisingly, we discovered that the majority of proteins involved in macroautophagy and several forms of microautophagy were dispensable for life-span extension. The only autophagy protein that is critical for life-span extension was Atg15, a lipase that is located in the endoplasmic reticulum (ER) and transported to vacuoles for disintegrating membranes of autophagic bodies. We further found that vacuole-vacuole fusion was required for life-span extension, which was indicated by the shortened life span of mutants missing proteins (ypt7Delta, nyv1Delta, vac8Delta) or lipids (erg6Delta) involved in fusion. Since a known function of vacuole-vacuole fusion is the maintenance of the vacuole membrane integrity, we analyzed aged vacuoles and discovered that aged cells had altered vacuolar morphology and accumulated autophagic bodies, suggesting that certain forms of autophagy do contribute to longevity. Like aged cells, erg6Delta accumulated autophagic bodies, which is likely caused by a defect in lipase instead of proteases due to the existence of multiple vacuolar proteases. Since macroautophagy is not blocked by erg6Delta, we propose that a new form of autophagy transports Atg15 via the fusion of vacuoles with vesicles derived from ER, and we designate this putative form of autophagy as secretophagy. Pending future biochemical studies, the concept of secretophagy may provide a mechanism for autophagy in life-span extension.

L2 ANSWER 3 OF 18 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:384147 CAPLUS
DOCUMENT NUMBER: 146:395262
TITLE: Individualized cancer treatments
INVENTOR(S): Lancaster, Jonathan M.; Nevins, Joseph R.
PATENT ASSIGNEE(S): H. Lee Moffitt Cancer Center, USA

SOURCE: PCT Int. Appl., 173pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007038792	A2	20070405	WO 2006-US38590	20060928
WO 2007038792	A9	20070607		
WO 2007038792	A3	20071122		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA				
CA 2624086	A1	20070405	CA 2006-2624086	20060928
US 20070172844	A1	20070726	US 2006-541165	20060928
PRIORITY APPLN. INFO.:				
			US 2005-721213P	P 20050928
			US 2005-731335P	P 20051028
			US 2006-778769P	P 20060303
			US 2006-779163P	P 20060303
			US 2006-779473P	P 20060306
			WO 2006-US38590	W 20060928

AB The invention provides for compns. and methods for predicting an individual's responsitivity to cancer treatments and methods of treating cancer. This invention relates to the use of gene expression profiling to determine whether an individual afflicted with cancer will respond to a therapy, and in particular to a therapeutic agents such as platinum-based agents. The invention also relates to the treatment of the individuals with the therapeutic agents. If the individual appears to be partially responsive or non-responsive to platinum-based therapy, then the individual's gene expression profile is used to determine which salvage agent should be used to further treat the individual to maximize cytotoxicity for the cancerous cells while minimizing toxicity for the individual. The invention also provides reagents, such as DNA microarrays, software and computer systems useful for personalizing cancer treatments, and provides methods of conducting a diagnostic business for personalizing cancer treatments.

L2 ANSWER 4 OF 18 MEDLINE on STN DUPLICATE 1
 ACCESSION NUMBER: 2007623605 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 17728253
 TITLE: Properties, regulation, and in vivo functions of a novel protein kinase D: Caenorhabditis elegans DKF-2 links diacylglycerol second messenger to the regulation of stress responses and life span.
 AUTHOR: Feng Hui; Ren Min; Chen Lu; Rubin Charles S
 CORPORATE SOURCE: Department of Molecular Pharmacology, Atran Laboratories, Albert Einstein College of Medicine, Bronx, New York 10461, USA.
 SOURCE: The Journal of biological chemistry, (2007 Oct 26) Vol. 282, No. 43, pp. 31273-88. Electronic Publication: 2007-08-29.

Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200712
ENTRY DATE: Entered STN: 24 Oct 2007
Last Updated on STN: 11 Dec 2007
Entered Medline: 6 Dec 2007

AB Protein kinase D (PKD) isoforms are protein kinase C effectors in signaling cascades controlled by diacylglycerol (DAG). All PKDs are regulated by DAG/phorbol 12-myristate 13-acetate-binding C1 domains and an activation loop (A-loop). To understand how PKD isoforms diversify DAG signaling networks, it is essential to determine redundant and novel properties of their regulatory domains, characterize factors controlling PKD gene expression, and discover their in vivo physiological roles. Studies on a novel PKD, *Caenorhabditis elegans* DKF-2 (D kinase family-2), addressed these topics. The C1b domain mediates phorbol 12-myristate 13-acetate-induced translocation and activation of DKF-2. However, when DAG is elevated, C1a and C1b contribute equally to targeting/activation of DKF-2. DKF-2 C1 domains do not inhibit catalytic activity; they mediate delivery of DKF-2 to a membrane where protein kinase C phosphorylates Ser(925) and Ser(929) in the A-loop. This potentially stimulates DKF-2 catalytic activity. Phosphorylation of Ser(925) alone switches on 70% of maximal kinase activity. Persistent phosphorylation of Ser(929) tags DKF-2 for proteasomal degradation; Ser(P)(925) plays a minor role in DKF-2 degradation. GATA enhancer sequences govern DKF-2 expression in intestine in vivo. Adult life span increases 40% in animals lacking DKF-2. In thermally stressed wild type animals, the DAF-16 transcription factor is segregated from the nuclei of adult intestinal cells. In contrast, DAF-16 enters adult intestinal nuclei of DKF-2-deficient, thermally stressed animals, where it can trigger gene transcription that protects against various insults. The results suggest a mechanism for increased longevity and show that a PKD links DAG signals to regulation of stress responses and life span.

L2 ANSWER 5 OF 18 MEDLINE on STN
ACCESSION NUMBER: 2007376355 MEDLINE
DOCUMENT NUMBER: PubMed ID: 17592521
TITLE: Involvement of genes required for synaptic function in aging control in *C. elegans*.
AUTHOR: Shen Lu-Lu; Wang Yang; Wang Da-Yong
CORPORATE SOURCE: Department of Genetics and Developmental Biology, Southeast University, Nanjing 210009, China.
SOURCE: Neuroscience bulletin, (2007 Jan) Vol. 23, No. 1, pp. 21-9. Journal code: 101256850. ISSN: 1673-7067.
PUB. COUNTRY: China
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200707
ENTRY DATE: Entered STN: 27 Jun 2007
Last Updated on STN: 1 Aug 2007
Entered Medline: 31 Jul 2007

AB OBJECTIVE: To identify new genes required for neurosecretory control of aging in *C. elegans*. METHODS: In view of the importance of nervous system in aging regulation, we performed the screen for genes involved in the aging regulation from genetic loci encoding synaptic proteins by lifespan assay and accumulation of lipofuscin autofluorescence. We further investigated the dauer formation phenotypes of their corresponding mutants

and whether they were possibly up-regulated by the insulin-like signaling pathway. RESULTS: The genetic loci of unc-10, syd-2, hlb-1, dlk-1, mkk-4, scd-2, snb-1, ric-4, nrx-1, unc-13, sbt-1 and unc-64 might be involved in the aging control. In addition, functions of unc-10, syd-2, hlb-1, dlk-1, mkk-4, scd-2, snb-1, ric-4 and nrx-1 in regulating aging may be opposite to those of unc-13, sbt-1 and unc-64. The intestinal autofluorescence assay further indicated that the identified long-lived and short-lived mutants were actually due to the suppressed or accelerated aging. Among the identified genes, syd-2, hlb-1, mkk-4, scd-2, snb-1, ric-4 and unc-64 were also involved in the control of dauer formation. Moreover, daf-2 mutation positively regulated the expression of syd-2 and hlb-1, and negatively regulated the expression of mkk-4, nrx-1, ric-4, sbt-1, rpm-1, unc-10, dlk-1 and unc-13. The daf-16 mutation positively regulated the expression of syd-2 and hlb-1, and negatively regulated the expression of mkk-4, nrx-1, sbt-1, rpm-1, unc-10, dlk-1 and unc-13. CONCLUSION: These data suggest the possibly important status of the synaptic transmission to the animal's life-span control machinery, as well as the dauer formation control.

L2 ANSWER 6 OF 18 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2006:1014641 CAPLUS

DOCUMENT NUMBER: 145:352139

TITLE: The insulin/PI 3-kinase pathway regulates salt chemotaxis learning in *Caenorhabditis elegans*

AUTHOR(S): Tomioka, Masahiro; Adachi, Takeshi; Suzuki, Hiroshi; Kunitomo, Hirofumi; Schafer, William R.; Iino, Yuichi

CORPORATE SOURCE: Molecular Genetics Research Laboratory, Graduate School of Science, The University of Tokyo, 7-3-1 Hongo, Bunkyo-ku Tokyo, 113-0033, Japan

SOURCE: Neuron (2006), 51(5), 613-625
CODEN: NERNET; ISSN: 0896-6273

PUBLISHER: Cell Press

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The insulin-like signaling pathway is known to regulate fat metabolism, dauer formation, and longevity in *Caenorhabditis elegans*. Here, the authors report that this pathway is also involved in salt chemotaxis learning, in which animals previously exposed to a chemoattractive salt under starvation conditions start to show salt avoidance behavior. Mutants of *ins-1*, *daf-2*, *age-1*, *pdk-1*, and *akt-1*, which encode the homologs of insulin, insulin/IGF-I receptor, PI 3-kinase, phosphoinositide-dependent kinase, and Akt/PKB, resp., show severe defects in salt chemotaxis learning. *Daf-2* and *age-1* act in the ASER salt-sensing neuron, and the activity level of the DAF-2/AGE-1 pathway in this neuron determines the extent and orientation of salt chemotaxis. *Ins-1* acts in AIA interneurons, which receive direct synaptic inputs from sensory neurons and also send synaptic outputs to ASER. These results suggest that *INS-1* secreted from AIA interneurons provides feedback to ASER to generate plasticity of chemotaxis.

REFERENCE COUNT: 80 THERE ARE 80 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 7 OF 18 MEDLINE on STN

ACCESSION NUMBER: 2005656363 MEDLINE

DOCUMENT NUMBER: PubMed ID: 16084636

TITLE: A 24-month dietary carcinogenicity study of DAG in mice.

AUTHOR: Chengelis Christopher P; Kirkpatrick Jeannie B; Bruner Richard H; Freshwater Les; Morita Osamu; Tamaki Yasushi; Suzuki Hiroyuki

CORPORATE SOURCE: WIL Research Laboratories, LLC, Ashland, OH 44805-9281,

SOURCE: USA.. chengelis@wilresearch.com
Food and chemical toxicology : an international journal
published for the British Industrial Biological Research
Association, (2006 Jan) Vol. 44, No. 1, pp. 122-37.
Electronic Publication: 2005-08-09.
Journal code: 8207483. ISSN: 0278-6915.

PUB. COUNTRY: England: United Kingdom

DOCUMENT TYPE: (COMPARATIVE STUDY)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200602

ENTRY DATE: Entered STN: 18 Dec 2005
Last Updated on STN: 10 Feb 2006
Entered Medline: 9 Feb 2006

AB This study evaluated the possible carcinogenic effects of DAG (diacylglycerol) oil when given in the diet at levels up to 6.0% for 24 months to mice. Dietary fat was provided by DAG and/or the control article, TG (triacylglycerol oil). Dietary concentrations (% DAG/% TG) were 0%/6.0% (TG control), 1.5%/4.5%, 3.0%/3.0%, and 6.0%/0%. An additional control group received the standard rodent diet (fat content 4.5%). The clinical condition of the animals, ophthalmic findings, palpable mass occurrence, body weights and gross and histopathologic findings were unaffected by DAG in comparison to TG. The findings in DAG-treated groups were no different than those observed in the TG control group. The standard basal diet had 4.5% fat content. Both TG and/or DAG, when presented separately or together in the diet at a total fat level of 6.0%, resulted in some differences relative to the basal diet control (lower survival, higher body weights, lower food consumption, and higher incidences of macroscopic and microscopic findings), presumably related to the higher dietary fat content and/or the semi-purified diet. However, these parameters were similar in groups fed a diet with 6.0% dietary fat that was either DAG or TG. Thus, DAG at dietary concentrations up to 6.0% for 24 months produced no signs of systemic toxicity and had no effect on the incidence of neoplastic findings.

L2 ANSWER 8 OF 18 MEDLINE on STN

ACCESSION NUMBER: 2005656365 MEDLINE

DOCUMENT NUMBER: PubMed ID: 16084639

TITLE: A 24-month dietary carcinogenicity study of DAG (diacylglycerol) in rats.

AUTHOR: Chengelis Christopher P; Kirkpatrick Jeannie B; Bruner Richard H; Freshwater Les; Morita Osamu; Tamaki Yasushi; Suzuki Hiroyuki

CORPORATE SOURCE: WIL Research Laboratories, LLC, Ashland, OH 44805-9281, USA.. chengelis@wilresearch.com

SOURCE: Food and chemical toxicology : an international journal
published for the British Industrial Biological Research
Association, (2006 Jan) Vol. 44, No. 1, pp. 98-121.
Electronic Publication: 2005-08-09.
Journal code: 8207483. ISSN: 0278-6915.

PUB. COUNTRY: England: United Kingdom

DOCUMENT TYPE: (COMPARATIVE STUDY)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200602

ENTRY DATE: Entered STN: 18 Dec 2005
Last Updated on STN: 10 Feb 2006

Entered Medline: 9 Feb 2006

AB Toxicologic and carcinogenic effects of DAG (diacylglycerol) oil, administered in diet for 24 months to Crl:CD((R)) (SD)-IGS BR rats, were evaluated using diet-restricted and ad libitum-fed groups. All dietary fat (consistently 5.5%) was provided by DAG and/or the control article, TG (triacylglycerol) oil. Dietary concentrations (% DAG/% TG) were 0%/5.5%, 1%/4.5%, 2.75%/2.75% and 5.5%/0%. Separate groups were fed the 0%/5.5% and 5.5%/0% diets ad libitum. Another group received the standard rodent diet (fat content 4.5%) on the restricted feeding regimen. Clinical condition, ophthalmic findings, palpable mass occurrence, body composition, clinical pathology parameters and incidence of neoplastic lesions were unaffected by DAG in comparison to TG. Groups fed the 5.5% (DAG and/or TG) fat diet when compared to the 4.5% fat diet group displayed lower survival, higher body weights, organ weights, percent body fat, higher fat-related serum chemistry parameters, incidence of microscopic changes in the heart, kidneys, liver, bone marrow, spleen, and incidences of pituitary and mammary gland neoplasms. Parameters more affected in all the ad libitum groups than in the restricted diet groups (regardless of test article) fed the same diet included survival, body weights, body fat, fat-related serum chemistry parameters, and incidences of heart, kidney and liver microscopic changes. However, the DAG and TG ad libitum-fed groups were not different from one another. Thus, DAG-treated animals had no higher risk of carcinogenic effects than rats fed on similar feeding regimens with a diet in which all dietary fat came from TG.

L2 ANSWER 9 OF 18 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2005:1276157 CAPLUS

DOCUMENT NUMBER: 145:77306

TITLE: Overlapping and distinct functions for a Caenorhabditis elegans SIR2 and DAF-16/FOXO

AUTHOR(S): Wang, Yamei; Tissenbaum, Heidi A.

CORPORATE SOURCE: Program in Gene Function and Expression, Program in Molecular Medicine, University of Massachusetts Medical School, Worcester, MA, 01605, USA

SOURCE: Mechanisms of Ageing and Development (2006), 127(1), 48-56

CODEN: MAGDA3; ISSN: 0047-6374

PUBLISHER: Elsevier Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The conserved SIR2 protein regulates life span in both yeast and worms: in both organisms overexpression of SIR2 can extend life span and in Caenorhabditis elegans this life span extension is dependent on the forkhead transcription factor, DAF-16. Here, we have done extensive genetic anal. with sir-2.1(ok434), a null mutant of C. elegans sir-2.1, the closest homolog to yeast Sir2p and human SIRT1 to further elucidate its function in life span regulation. sir-2.1(ok434) mutants show a slight decrease in life span as well as sensitivity to various stresses. Our genetic anal. suggests that sir-2.1 is required for life span extension by caloric restriction, independent of the insulin/IGF-1 signaling pathway. Importantly, anal. with unc-13 mutants indicates that sir-2.1 and daf-16 have overlapping and distinct roles in life span regulation. Our expression anal. shows that sir-2.1 has overlapping and distinct expression pattern compared with daf-16, consistent with the results from our genetic data. Our data defines a central role for C. elegans SIR2 in regulation of life span by caloric restriction and demonstrates that sir-2.1 and daf-16 have both overlapping and distinct functions in regulation of C. elegans life span.

REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 10 OF 18 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN

ACCESSION NUMBER: 2005:419702 BIOSIS
DOCUMENT NUMBER: PREV200510211301
TITLE: Longevity record for Snares Island
snipe (*Coenocorypha aucklandica huegeli*).
AUTHOR(S): Miskelly, Colin M. [Reprint Author]; Sagar, Paul M.
CORPORATE SOURCE: Wellington Conservancy, Dept Conservat, POB 5086,
Wellington, New Zealand
cmiskelly@doc.govt.nz
SOURCE: Notornis, (JUN 2005) Vol. 52, No. Part 2, pp. 120-121.
ISSN: 0029-4470.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 19 Oct 2005
Last Updated on STN: 19 Oct 2005

L2 ANSWER 11 OF 18 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2004:857688 CAPLUS
DOCUMENT NUMBER: 141:343538
TITLE: Neurotransmitter signaling can regulate life span in
Caenorhabditis elegans, and methods of identifying
modulators of longevity
INVENTOR(S): Tissenbaum, Heidi A.
PATENT ASSIGNEE(S): University of Massachusetts, USA
SOURCE: PCT Int. Appl., 87 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004087888	A2	20041014	WO 2004-US9882	20040329
WO 2004087888	A3	20050310		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
US 20050044579	A1	20050224	US 2004-813324	20040329
PRIORITY APPLN. INFO.:			US 2003-459079P	P 20030327

AB The invention discloses methods of identifying modulators of longevity. Also discloses are organisms, cell systems, and compns. for performing those methods. Further discloses are therapeutic methods for the use of modulators identified according to the methods.

L2 ANSWER 12 OF 18 MEDLINE on STN

DUPLICATE 2

ACCESSION NUMBER: 2003016436 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12381720
TITLE: Evaluation of the therapeutic usefulness of botulinum neurotoxin B, C1, E, and F compared with the long lasting type A. Basis for distinct durations of inhibition of exocytosis in central neurons.

AUTHOR: Foran Patrick G; Mohammed Nadiem; Lisk Godfrey O; Nagwaney Sharuna; Lawrence Gary W; Johnson Eric; Smith Leonard; Aoki K Roger; Dolly J Oliver
CORPORATE SOURCE: Centre for Neurobiochemistry, Department of Biological Sciences, Imperial College, London SW7 2AZ, United Kingdom.
SOURCE: The Journal of biological chemistry, (2003 Jan 10) Vol. 278, No. 2, pp. 1363-71. Electronic Publication: 2002-10-14.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: (COMPARATIVE STUDY)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, NON-P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200303
ENTRY DATE: Entered STN: 14 Jan 2003
Last Updated on STN: 8 Mar 2003
Entered Medline: 7 Mar 2003

AB Seven types (A-G) of botulinum neurotoxin (BoNT) target peripheral cholinergic neurons where they selectively proteolyze SNAP-25 (BoNT/A, BoNT/C1, and BoNT/E), syntaxin1 (BoNT/C1), and synaptobrevin (BoNT/B, BoNT/D, BoNT/F, and BoNT/G), SNARE proteins responsible for transmitter release, to cause neuromuscular paralysis but of different durations. BoNT/A paralysis lasts longest (4-6 months) in humans, hence its widespread clinical use for the treatment of dystonias. Molecular mechanisms underlying these distinct inhibitory patterns were deciphered in rat cerebellar neurons by quantifying the half-life of the effect of each toxin, the speed of replenishment of their substrates, and the degradation of the cleaved products, experiments not readily feasible at motor nerve endings. Correlation of target cleavage with blockade of transmitter release yielded half-lives of inhibition for BoNT/A, BoNT/C1, BoNT/B, BoNT/F, and BoNT/E (31, 25, approximately 10, approximately 2, and approximately 0.8 days, respectively), equivalent to the neuromuscular paralysis times found in mice, with recovery of release coinciding with reappearance of the intact SNAREs. A limiting factor for the short neuromuscular durations of BoNT/F and BoNT/E is the replenishment of synaptobrevin or SNAP-25, whereas pulse labeling revealed that extended inhibition by BoNT/A, BoNT/B, or BoNT/C1 results from longevity of each protease. These novel findings could aid development of new toxin therapies for patients resistant to BoNT/A and effective treatments for human botulism.

L2 ANSWER 13 OF 18 MEDLINE on STN
ACCESSION NUMBER: 2003611864 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14694798
TITLE: [Unequal chances for reaching 'a good old age'.
Socio-economic health differences among older adults from a life course perspective].
Ongelijke kansen op een goede oude dag.
Sociaal-economische gezondheidsverschillen bij ouderen vanuit een levensloopperspectief.
AUTHOR: Broese van Groenou Marjolein I
CORPORATE SOURCE: Afdeling Sociaal-Culturele Wetenschappen, Faculteit der Sociale Wetenschappen, Vrije Universiteit, De Boelelaan 1081c, 1081 HV Amsterdam.. mi.broese@fsw.vu.nl
SOURCE: Tijdschrift voor gerontologie en geriatrie, (2003 Oct) Vol. 34, No. 5, pp. 196-207.
Journal code: 8210346. ISSN: 0167-9228.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: (COMPARATIVE STUDY)

(ENGLISH ABSTRACT)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)

LANGUAGE: Dutch
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200402
ENTRY DATE: Entered STN: 26 Dec 2003
Last Updated on STN: 18 Feb 2004
Entered Medline: 17 Feb 2004

AB This article provides an overview of the socioeconomic inequality in physical and psychological health of older adults between 55 and 85 years of age, with a focus on the older adults whose socioeconomic status (SES) remains at a low level all their life. Data are derived from 1471 men and 1568 women, participating in the Longitudinal Aging Study Amsterdam (LASA) in 1992/1993. Based on the parental and own level of education, respondents are divided in four categories: those with a life time low level of SES, those with downward or upward mobility in SES, and those with a life time high level of SES. Logistic regression analyses showed that older adults with upward SES mobility and life time high SES, had a lower risk for functional limitations, chronic diseases (men only), 6-year mortality, depression and loneliness, compared with the older adults with life time low SES. The disadvantaged position of the low SES persons with regard to age, health and psychosocial conditions explained the SES differences in depression, but SES differences in mortality (for men) and in functional disability (for men and women) are not explained by the risk factors under study. SES differences in loneliness were attributed to differences in psychosocial conditions. Lifestyle did not add to the explanation of any of the SES differences. There were only small differences between those with a life time low SES and those with downward mobility in SES. It is concluded that a low level of education (regardless of the parental level) contributes to restricted psychosocial conditions, health problems and low well-being in old age, thereby decreasing the chances for a 'good old age' considerably.

L2 ANSWER 14 OF 18 MEDLINE on STN DUPLICATE 3
ACCESSION NUMBER: 2003075628 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12586705
TITLE: Positive selection of *Caenorhabditis elegans* mutants with increased stress resistance and longevity.
AUTHOR: Munoz Manuel J; Riddle Donald L
CORPORATE SOURCE: Molecular Biology Program and Division of Biological Sciences, University of Missouri, Columbia, Missouri 65211-7400, USA.
CONTRACT NUMBER: AG12689 (United States NIA)
GM60151 (United States NIGMS)
SOURCE: Genetics, (2003 Jan) Vol. 163, No. 1, pp. 171-80.
Journal code: 0374636. ISSN: 0016-6731.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200309
ENTRY DATE: Entered STN: 15 Feb 2003
Last Updated on STN: 13 Sep 2003
Entered Medline: 12 Sep 2003

AB We developed selective conditions for long-lived mutants of the nematode *Caenorhabditis elegans* by subjecting the first larval stage (L1) to thermal stress at 30 degrees for 7 days. The surviving larvae developed to fertile adults after the temperature was shifted to 15 degrees. A total of one million F(2) progeny and a half million F(3) progeny of

ethyl-methanesulfonate-mutagenized animals were treated in three separate experiments. Among the 81 putative mutants that recovered and matured to the reproductive adult, 63 retested as thermotolerant and 49 (80%) exhibited a >15% increase in mean life span. All the known classes of dauer formation (Daf) mutant that affect longevity were found, including six new alleles of daf-2, and a unique temperature-sensitive, dauer-constitutive allele of age-1. Alleles of dyf-2 and unc-13 were isolated, and mutants of unc-18, a gene that interacts with unc-13, were also found to be long lived. Thirteen additional mutations define at least four new genes.

L2 ANSWER 15 OF 18 MEDLINE on STN DUPLICATE 4
 ACCESSION NUMBER: 2000395723 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 10747056
 TITLE: Genetic, behavioral and environmental determinants of male longevity in *Caenorhabditis elegans*.
 AUTHOR: Gems D; Riddle D L
 CORPORATE SOURCE: The Galton Laboratory, Department of Biology, University College London, England.. d.gems@galton.ucl.ac.uk
 CONTRACT NUMBER: AG12689 (United States NIA)
 SOURCE: Genetics, (2000 Apr) Vol. 154, No. 4, pp. 1597-610. Journal code: 0374636. ISSN: 0016-6731.
 PUB. COUNTRY: United States
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T) (RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 200008
 ENTRY DATE: Entered STN: 24 Aug 2000
 Last Updated on STN: 24 Aug 2000
 Entered Medline: 16 Aug 2000

AB Males of the nematode *Caenorhabditis elegans* are shorter lived than hermaphrodites when maintained in single-sex groups. We observed that groups of young males form clumps and that solitary males live longer, indicating that male-male interactions reduce life span. By contrast, grouped or isolated hermaphrodites exhibited the same longevity. In one wild isolate of *C. elegans*, AB2, there was evidence of copulation between males. Nine uncoordinated (unc) mutations were used to block clumping behavior. These mutations had little effect on hermaphrodite life span in most cases, yet many increased male longevity even beyond that of solitary wild-type males. In one case, the neuronal function mutant unc-64(e246), hermaphrodite life span was also increased by up to 60%. The longevity of unc-4(e120), unc-13(e51), and unc-32(e189) males exceeded that of hermaphrodites by 70-120%. This difference appears to reflect a difference in sex-specific life span potential revealed in the absence of male behavior that is detrimental to survival. The greater longevity of males appears not to be affected by daf-2, but is influenced by daf-16. In the absence of male-male interactions, median (but not maximum) male life span was variable. This variability was reduced when dead bacteria were used as food. Maintenance on dead bacteria extended both male and hermaphrodite longevity.

L2 ANSWER 16 OF 18 MEDLINE on STN
 ACCESSION NUMBER: 2000031221 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 10566945
 TITLE: Retention of cleaved synaptosome-associated protein of 25 kDa (SNAP-25) in neuromuscular junctions: a new hypothesis to explain persistence of botulinum A poisoning.
 AUTHOR: Raciborska D A; Charlton M P
 CORPORATE SOURCE: Department of Physiology, University of Toronto, ON,

Canada.
SOURCE: Canadian journal of physiology and pharmacology, (1999 Sep)
Vol. 77, No. 9, pp. 679-88.
Journal code: 0372712. ISSN: 0008-4212.
PUB. COUNTRY: Canada
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199911
ENTRY DATE: Entered STN: 13 Jan 2000
Last Updated on STN: 13 Jan 2000
Entered Medline: 30 Nov 1999

AB Botulinum neurotoxins can block neurotransmitter release for several months. The molecular mechanism of these toxins' action is known, but the persistence of neuromuscular paralysis that they cause is unexplained. At frog neuromuscular junctions, application of botulinum toxin type A caused paralysis and reduced the C-terminus immunoreactivity of SNAP-25, but not that of the remaining N-terminus fragment. Botulinum toxin type C caused paralysis and reduced syntaxin immunoreactivity without affecting that of SNAP-25. Co-application of botulinum A and C reduced syntaxin immunoreactivity, and that of both C and N termini of SNAP-25. Application of hydroxylamine to de-palmitoylate SNAP-25 resulted in a slight reduction of the immunoreactivity of SNAP-25 N terminus, while it had no effect on immunoreactivity of botulinum A cleaved SNAP-25. In contrast, application of hydroxylamine to nerve terminals where syntaxin had been cleaved by botulinum C caused a considerable reduction in SNAP-25 N-terminus immunoreactivity. Hence the retention of immunoreactive SNAP-25 at the neuromuscular junction depends on its interactions with syntaxin and plasma membrane. Persistence of cleaved SNAP-25 in nerve terminals may prevent insertion of new SNAP-25 molecules, thereby contributing to the longevity of botulinum A effects.

L2 ANSWER 17 OF 18 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN

ACCESSION NUMBER: 1996:469966 BIOSIS
DOCUMENT NUMBER: PREV199699192322
TITLE: Sperm quality improvement in cryopreserved human semen.
AUTHOR(S): Sharma, Rakesh K.; Agarwal, Ashok [Reprint author]
CORPORATE SOURCE: Androl. Res. Clin. Lab., Dep. Urol., A100, Cleveland Clin. Foundation, 9500 Euclid Ave., Cleveland, OH 44195, USA
SOURCE: Journal of Urology, (1996) Vol. 156, No. 3, pp. 1008-1012.
CODEN: JOURAA. ISSN: 0022-5347.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 11 Oct 1996
Last Updated on STN: 11 Oct 1996

AB Purpose: We determined if separation of spermatozoa (washed) on a discontinuous colloidal suspension of silica (Percoll dag) density gradient before cryopreservation improves post-thaw motility compared to an unprocessed (raw) cryopreserved sample. Materials and Methods: Ten normal healthy volunteers recruited into the andrology laboratory donor program were studied. Raw and washed cryopreserved spermatozoa were compared for loss of motility with time, motion characteristics, viability and membrane integrity after incubation for 1, 6 and 24 hours. Within-group comparisons were made to baseline measurements (0 hours before incubation). Results: Raw and washed cryopreserved spermatozoa showed statistically significant decreases in motility and other motion characteristics after thawing. There were significant decreases in motility and other motion characteristics after incubation periods of 1, 6 and 24 hours, and significant decreases in viability and membrane integrity at 6 and 24 hours in the unprocessed

spermatozoa. Although, motility and motion characteristics of washed samples decreased significantly with longer incubation periods, loss of motility with time (longevity) was greater in raw samples. Washed samples retained greater sperm motility for up to 24 hours (p lt 0.03). Conclusions: Specimens prepared by Percoll separation techniques before freezing offer the possibility of selecting spermatozoa that retain motility for up to 24 hours. This finding can be of benefit for couples undergoing intrauterine insemination to achieve pregnancy.

L2 ANSWER 18 OF 18 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on
STN DUPLICATE 5

ACCESSION NUMBER: 1996:460031 BIOSIS
DOCUMENT NUMBER: PREV199699182387
TITLE: Photosynthesis, growth and nutrient changes in
non-nodulated Phaseolus vulgaris grown under atmospheric
and elevated carbon dioxide conditions.
AUTHOR(S): Mjwara, Jabulani M. [Reprint author]; Botha, C. Edward J.;
Radloff, Sarah E.
CORPORATE SOURCE: Schoenland Botanical Lab., Botany Dep., Rhodes Univ., P.O.
Box 94, Grahamstown 6140, South Africa
SOURCE: Physiologia Plantarum, (1996) Vol. 97, No. 4, pp. 754-763.
CODEN: PHPLAI. ISSN: 0031-9317.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 11 Oct 1996
Last Updated on STN: 11 Oct 1996

AB The response of Phaseolus vulgaris L. cv. Contender grown under
controlled environment at either ambient or elevated (360 and 700 μ -mol
mol⁻¹, respectively) CO-2 concentrations ((CO-2)), was monitored from 10
days after germination (DAG) until the onset of senescence.
Elevated CO-2 had a pronounced effect on total plant height (TPH), leaf
area (LA), leaf dry weight (LD), total plant biomass (TB) accumulation and
specific leaf area (SLA). All of these were significantly increased under
elevated carbon dioxide with the exception of SLA which was significantly
reduced. Other than high initial growth rates in CO-2-enriched plants,
relative growth rates remained relatively unchanged throughout the growth
period. While the trends in growth parameters were clearly different
between (CO-2), some physiological processes were largely transient, in
particular, net assimilation rate (NAR) and foliar nutrient concentrations
of N, Mg and Cu. CO-2 enrichment significantly increased NAR, but from 20
DAG, a steady decline to almost similar levels to those measured
in plants grown under ambient CO-2 occurred. A similar trend was observed
for leaf N content where the loss of leaf nitrogen in CO-2-enriched plants
after 20 DAG, was significantly greater than that observed for
ambient-CO-2 plants. Under enhanced CO-2, the foliar concentrations of K
and Mn were increased significantly whilst P, Ca, Fe and Zn were reduced
significantly. Changes in Mg and Cu concentrations were insignificant.
In addition, high CO-2 grown plants exhibited a pronounced leaf
discoloration or chlorosis, coupled with a significant reduction in leaf
longevity.

=> FIL STNGUIDE

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	ENTRY	SESSION
FULL ESTIMATED COST	64.86	65.07
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL
	ENTRY	SESSION
CA SUBSCRIBER PRICE	-3.20	-3.20

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"HELP COMMANDS" at an arrow prompt (=>).

=> logoff
ALL L# QUERIES AND ANSWER SETS ARE DELETED AT LOGOFF
LOGOFF? (Y)/N/HOLD:y
COST IN U.S. DOLLARS

	SINCE FILE	TOTAL
	ENTRY	SESSION
FULL ESTIMATED COST	1.14	66.21
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)		
	SINCE FILE	TOTAL
	ENTRY	SESSION
CA SUBSCRIBER PRICE	0.00	-3.20

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